A STUDY ON CLINICAL PROFILE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASES

Dissertation submitted to

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GENERAL MEDICINE

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MARCH 2008

CERTIFICATE

This is to certify that the dissertation titled **"A STUDY ON CLINICAL PROFILE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASES"** is the bonafide original work of **DR.S.SUDHASELVI,** in partial fulfillment of the requirements for M.D. Branch – I (General Medicine) Examination of the Tamilnadu DR. M.G.R Medical University to be held in MARCH 2008. The Period of study was from November 2006 to June 2007.

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DECLARATION

I, **DR.S.SUDHASELVI,** solemnly declare that dissertation titled **"A STUDY ON CLINICAL PROFILE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASES"** is a bonafide record of work done by me in the Department of Internal Medicine, Government Stanley Medical College and Hospital during November 2006 to June 2007 under the guidance of **Prof.T.VENKATAKRISHNAN, M.D.,** Professor of Medicine, Government Stanley Medical College and Hospital, Chennai.

This dissertation is submitted to Tamilnadu DR. M.G.R Medical University, in partial fulfillment of the University regulations for the award of **M.D. Degree (Branch – I) in General Medicine – March 2008.**

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CONTENTS

ABBREVIATIONS

COPD : Chronic Obstructive Pulmonary Disease

RTIs : Respiratory Tract Infections

IL : Inter Leukins

GM-CSF : Granulocyte Macrophage Colony Stimulating Factor

CRP : C-Reactive Protein

TNF-α : Tumor Necrosis Factor

GFR : Glomerular Filtration Rate

PH : Pulmonary Hypertension

SHS : Second hand smoke

Normal Values

P^H : 7.35 – 7.45

PO_2 : 75 – 100 mmHg

PCO_2 : 36 – 46 mmHg

HCO_3 : 22 – 26 meq/L

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is defined as a disease state characterized by the presence of airflow obstruction due to chronic bronchitis or emphysema; airflow obstruction is generally progressive, may be accompanied by airway reactivity and may be partially reversible.

Chronic Obstructive Pulmonary Disease (COPD) causes significant mortality and morbidity all over the world. Death rate from the disease has increased in recent decades in apparent association with smoking and air pollution.

Various synonyms for COPD

1. Chronic Obstructive Airway Disease (COAD).

2. Chronic Obstructive Lung Disease (COLD).

AIM OF THE STUDY

1. To study various risk factors associated with Chronic Obstructive Pulmonary Disease (COPD).

2. To evaluate biochemical, radiological, electrocardiographic, spirometric, Echocardiographic, ABG (Arterial Blood Gas) aspect of Chronic Obstructive Pulmonary Disease (COPD).

REVIEW OF THE LITERATURE

Chronic Obstructive Pulmonary Disease (COPD) has been defined by the Global Initiative for Chronic Obstructive Lung Diseases (GOLD) as a disease state characterized by airflow limitation that is not fully reversible[1].

Chronic Obstructive Pulmonary Disease (COPD) is present only if chronic airflow obstruction occurs. The definition excludes chronic bronchitis without chronic airflow obstruction. Other causes of a chronic airflow obstruction such as cystic fibrosis, bronchiolitis obliterans and bronchiectasis, carcinoma of lung, chronic congestive heart failure[1].

Chronic Obstructive Pulmonary Disease (COPD) may coexist with asthma and when abnormal airway reactivity is preexist, differentiation between these disorders can be challenging.

Chronic Obstructive Pulmonary Disease (COPD) comprises emphysema and chronic bronchitis, two direct processes, although most often present in combination.

Chronic bronchitis is defined as the presence of chronic productive cough for three months during each of two successive years in a patient in whom the other causes of chronic cough have been excluded[2,3].

Emphysema defined as abnormal permanent enlargement of distal air spaces distal to terminal bronchioles, accompanied by destruction of their walls and without obvious fibrosis[3]. The pathological hallmarks of chronic obstructive pulmonary disease are inflammation of the small airways

(bronchiolitis) and destruction of lung parenchyma (emphysema). The functional consequences of these abnormalities is airflow limitation[4,5].

The BTS(BritishThoracicSocietyguidelines) suggest that a diagnosis in clinical practice is usually associated with:

1. A history of chronic progressive symptoms (cough, wheeze and / or breathlessness) with little variation.

2. Usually a cigarette smoking history of greater than 20 pack year (1 pack year is equivalent to smoking 20 cigarettes a day for 1 year).

3. Objective evidence of air ways obstruction, ideally by spirometry that does not return to normal with treatment.

4. Chronic bronchitis has been classified into 3 form[5].

    a. Simple bronchitis, defined as hyper secretion of mucus.

    b. Chronic or recurrent mucopurulent bronchitis in the presence of persistent or intermittent mucopurulent sputum.

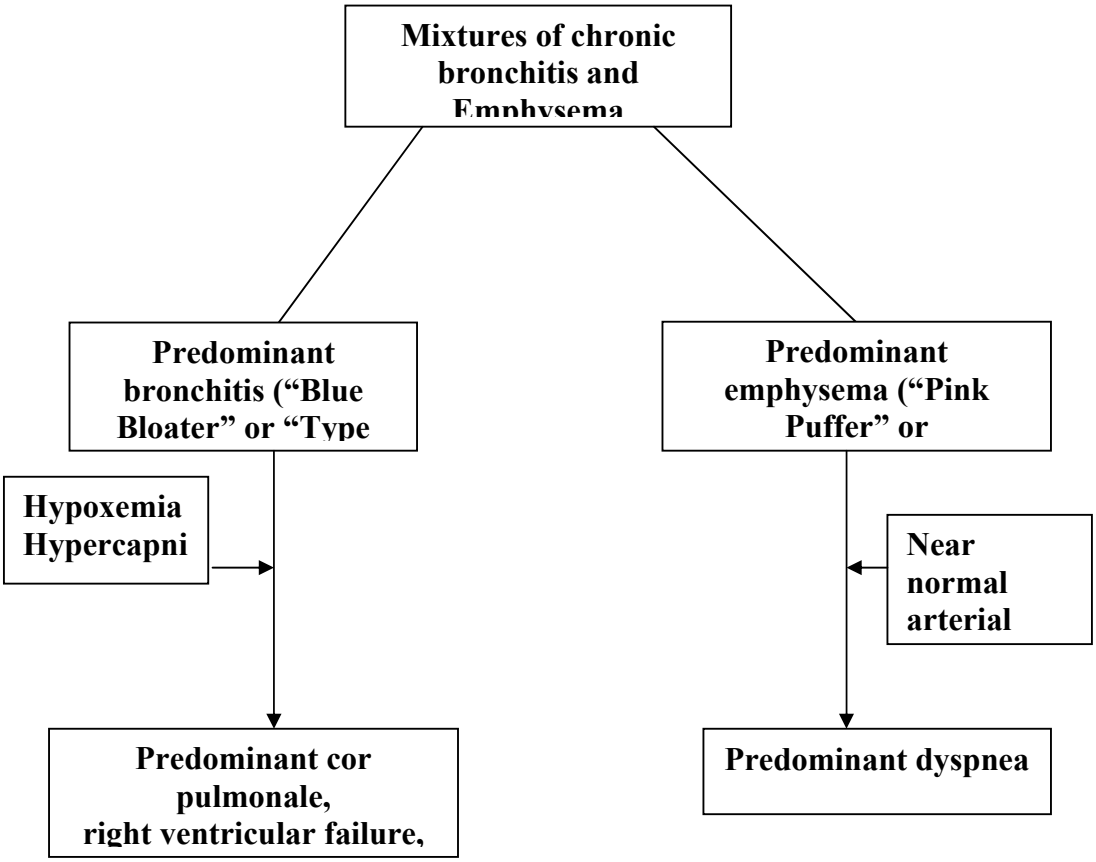
    c. Chronic obstructive bronchitis when chronic sputum production is associated with airflow obstruction.

DIFFERENCE BETWEEN CHRONIC BRONCHITIS AND EMPHYSEMA

TABLE : FISHMAN

Clinical Hallmarks	Predominant Bronchitis	Predominant Emphysema
1. General Appearance	Mesomorphic; over weight; dusky with suffused conjunctiva: warm extremities	Thin, often emaciated, pursed lip breaths, anxious, prominent use of accessory muscle normal or cool extremities.
2. Age	40 – 55	50 – 75
3. Onset	Cough	Dyspnoea
4. Cyanosis	Marked	Slight to none
5. Sputum	Copious	Scanty
6. Breath sound	Moderately diminished	Markedly diminished
7. Corpulmonale	Common	Only during bout of respiratory infection and terminally
8. Radiograph	Normal diaphragm position; cardiomegaly; lungs normal or with increased bronchovascular markings.	Small pendulous heart; low flat diaphragms; areas of increased radiolucency
9. FEV1/VC	Reduced	Reduced
10. FRC	Mildly increased	Markedly increased
11. TLC	Normal or slightly increased	Considerably increased
12. RV	Moderately increased	Markedly increased

BLUE BLOATER VERSUS PINK PUFFER



EPIDEMIOLOGY

Chronic Obstructive Pulmonary Disease (COPD) is a common medical problem which is worldwide in prevalence. They are extremely common in India. Here, they account for approximately 1/3 of patient seen in the chest clinic of general hospitals.

Disease is seen in mostly males over the age of 40 years who have been chronic and heavy smokers. It may occasionally be seen in non-smoker who have been exposed to prolonged atmospheric pollution.

An increased risk for the development of Chronic Obstructive Pulmonary Disease (COPD) in individuals of lower socio economic status, possible mechanism to explain the socio economic effect include crowded living conditional, increased incidence of Respiratory Tract Infections (RTIs). Nutritional status, birth weight and weight at one year of age are significant risk factors for later Chronic Obstructive Pulmonary Disease (COPD) and may be surrogate markers for socio economic status.

Feenstra et al, recently showed that there will be increase in burden of COPD between 1994 – 2015. This will result in a 43% increase in prevalence of COPD for males and 42% increase for females[52].

RISK FACTORS

TABLE 1

RISK FACTORS FOR THE DEVELOPMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Host susceptibility Factors	Environmental risk factors
Age	Smoking
Airway responsiveness	Occupational exposure
Allergy	(Indoor) Air pollution (wood smoke, chronic bio mass)
Sex	Diet
Genetics	Environmental allergens

- Risk considerations in Chronic Obstructive Pulmonary Disease (COPD) should be divided into (a) risk for disease development and (b) risk for disease progression.

- Risk for disease development includes **(Table 1)**

- Child-hood asthma and increased airways responsiveness may also represent the most important events that mark susceptibility for lung function decline and subsequent development of Chronic Obstructive Pulmonary Disease (COPD)

- Asthmatic type symptoms tend to decline with lung growth.

- Airway Hyper responsiveness, risk factor for both development and disease progression.

1. Smoking

Cigarette smoking is the major risk factors associated with the development of Chronic Obstructive Pulmonary Disease (COPD). All patients with chronically significant emphysema are smokers. Heavy smokers are greater risk of developing Chronic Obstructive Pulmonary Disease (COPD) than moderate smokers[6]. Passive smoking also seems to be harmful. The rate of expiratory airflow in cigarette smokers, decreases twice as fast in smokers (40 ml a year) as in non-smokers. (20 ml a year)[6].

Cigarette smoking is clearly the single most important identifiable aetiological factor in Chronic Obstructive Pulmonary Disease (COPD). However, only 10 – 20% of smokers develop clinically significant Chronic Obstructive Pulmonary Disease (COPD) while approximately half never develop a clinically significant physiological deficit[7].

Factors involved in smoking related Chronic Obstructive Pulmonary Disease (COPD) includes:

1. Genetic predisposition
2. Female Sex
3. Presence of underlying Asthma
4. Airway responsiveness
5. Possible, the presence of Allergy[8]

Although it is generally regarded as the dominant risk factor, cigarette smoking is not prerequisite in all definitions of Chronic Obstructive Pulmonary Disease (COPD) since COPD can occur in non-smokers such as patient with α1 antitrypsin deficiency.

The effects of smoking cessation on mortality have been less clear. Randomized controlled trials fail to demonstrate a unequivocal benefit in terms of respiratory mortality from stopping smoking[8].

Passive Smoking or Second Hand Smoke (SHS)

Relationship between passive smoking and chronic airflow obstruction has been examined using case – control[9] and a cohort study[10,58]. These studies shows a trend towards an increased relative risk from passive smokers, similar to that of lung cancer but not powerful enough to demonstrate statistical significance. SHS is a modifiable risk factor and it is determined with urine 4 methyl nitrosamine, serum cotinine level in blood.

i. Current smoking defined as regular cigarette smoking ie. at least 5 cigarettes a week almost every week for atleast 3 months serum cotinine level > 15 ng/ml.Previous smokers who denied current smoking with previously using cigarettes.

ii. Never smoking with positive passive smoke exposure serum cotinine level < 15ng/ml.

iii. Never smokers with negative passive smoking serum cotinine is usually undetectable.

Passive smoking causes injury to respiratory system with the finding of combined increased mortality risk for men and women for COPD. Public health counselling, laws prohibiting public smoking is must for prevention of its hazards.

2. Air Pollution

Several studies in 1950s, 1960s and early 1970s produced evidence incriminating air pollution as an etiological factor in COPD, including:

i. The association, in the UK, between increasing mortality and prevalence of COPD and increasing urbanization[11].

ii. The close association between atmospheric pollution and mortality from COPD both geographically and temporally[12].

iii. The demonstration that post office employees in foggy areas showed a higher rate of susceptibility than those working in less foggy areas[13].

iv. The increased in reported symptoms of chronic bronchitis in areas of increased air pollution[14].

v. A higher prevalence of emphysema in autopsy studies in areas with greater pollution[14].

3. Occupation

It is generally accepted that there is a causal link between occupational dust exposure and development of mucous hyper secretion[15].

Chronic bronchitis is more prevalent in workers who engage in occupations exposing them to either inorganic or organic dust or to noxious gases.

4. Genetics

Most COPD is not secondary to α1 antitrypsin deficiency, the only currently proven genetic risk for the diseases. Instead, most COPD represents the expression of a complex genetic disease resulting from an interaction between host and environmental factors.

5. Gender and Socio economic status

Most population studies have reported a higher prevalence of respiratory symptoms in men than in women[10]. But the prevalence gap between male and female is narrowing due to increased rate of cigarette smoking in the last 20 – 30 years. Females are more susceptible to the effect of smoking than males since female have lower FEV_1 than male.

ROLE OF INFECTIONS

Morbidity, mortality and frequency of acute respiratory infection are higher in patients with chronic bronchitis. Epidemiologic studies implicate acute respiratory illness as one of the major factors associated with etiology and progression of COPD[16].

Infections is a common precipitating factor, although only 50% of patients with severe exacerbation with associated respiratory failure have a positive sputum culture for a bacterium[17]. The commonest organism are H. Influenezae and streptococcus pneumoniae[17] although more recently moraxella catarrhalis has also been shown to be a common pathogen[18]. However, patient with COPD are often chronically colonized with common bacterial pathogens and therefore culture of one of these organism during acute exacerbation does not imply that this organism is responsible for exacerbation. Some studies have demonstrated an increased antibody titre of H.influenzae following exacerbation, suggesting that this organisms is causally involved[19].

Viral infections have been shown to be responsible for up to 30% of all exacerbation of COPD. This may well be an underestimate due to difficulties in viral isolation. In view of relatively limited number of pathogen, it has been considered that bacteriological examination of the sputum may not influence the management in an acute exacerbation of COPD although this is controversial[20,21,22].

PATHOGENESIS

COPD evolves from an inflammatory process involving the airways and distal airspaces. The protease and antiprotease hypothesis holds that destruction of alveolar walls stems from an imbalance between protease and their inhibitors in the lung.

The evidence is as follows[23].

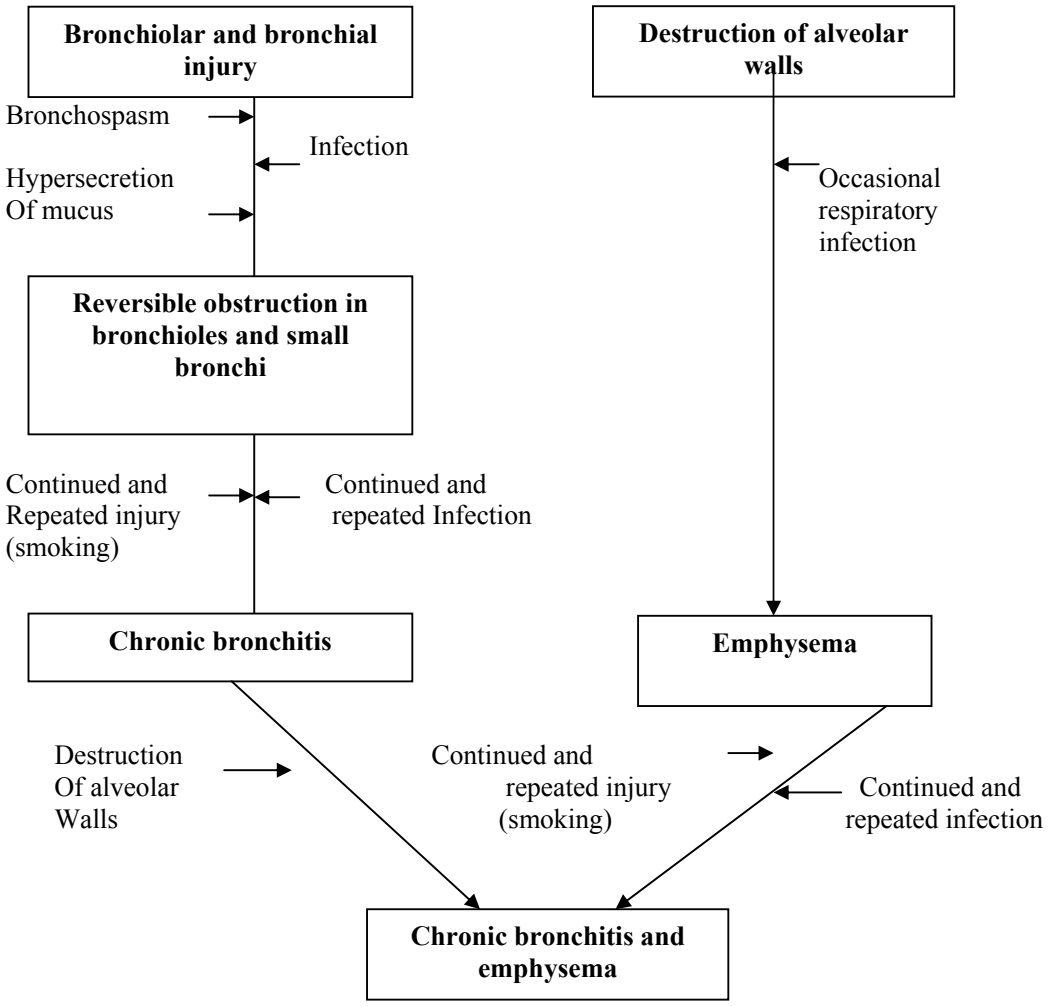
i. Individuals with hereditary deficiency of the major protease inhibitor α-1 antitrypsin, invariably develop emphysema and at a younger age if they smoke.

ii. Pulmonary instillation of proteolytic enzymes, includes neutrophil elastase, results in emphysema in experimental animals.

Tobacco smoking contributes toemphysema by:

1. Recruiting neutrophils into the lung by factors from smoke activated alveolar macrophages.
2. Stimulating release of elastase from neutrophils.
3. Enhancing macrophage elastase activity
4. Inactivation of α 1 antitrypsin by oxidants in tobacco smoke or free radicals released by activated neutrophils.

SCHEMATIC REPRESENTATION OF THE EVOLUTION OF CHRONIC BRONCHITIS AND EMPHYSEMA



PATHOLOGY

Emphysema

It is further classified according to the anatomic distribution of the lesion within the acinus[23].

1. Centri acinar Emphysema

It is characterized by

a) Destruction and enlargement of the central or proximal parts of the respiratory unit – the acinus – sparing distal alveoli.

b) Predominant involvement of upper lobes and apices. Severe lesions are seen primarily in male smokes, often in association with chronic bronchitis.

2. Pan acinar Emphysema

It is characterized by

a) Uniform destruction and enlargement of the acinus

b) Predominance of lower basal zones.

c) Strong association with α1 – antitrypsin deficiency.

3. Paraseptal Emphysema

Paraseptal emphysema involves mostly the distal acinus sparing the proximal and:

a. Is found near the pleura and adjacent to fibrosis or scars.

b. Is often the underlying lesion of spontaneous pneumothorax.

4. Irregular emphysema

Irregular emphysema refers to irregular involvement of the acinus. usually asymptomatic.

Other types are bullous emphysema and interstitial emphysema.

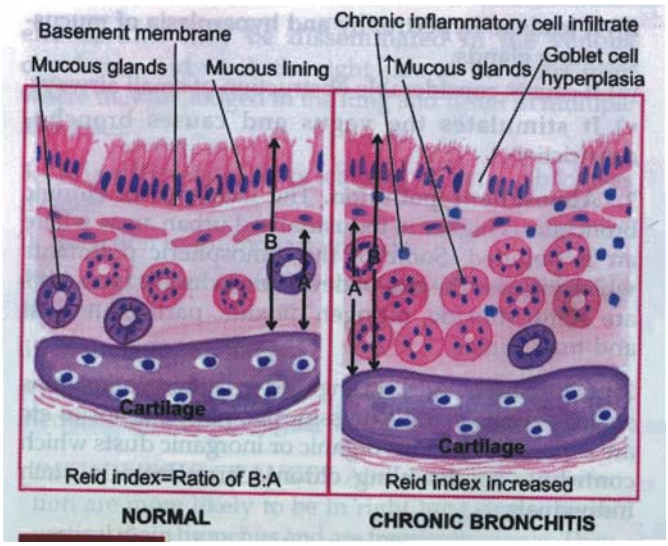
CHRONIC BRONCHITIS

It is characterized by

- Hyperemia and edema of mucous membrane of the lung
- Mucinous secretion or cast filling airways.
- Increase in size of the mucous glands
- Bronchial or bronchiolar mucous plugging, inflammation and fibrosis.
- Squamous metaplasia or dysplasia of bronchial epithelium.
- Mucous gland hypertrophy can be quantified by the Reid Index[23]. It is ratio of the thickness of submucosal glands to that of the bronchial wall.

Reid Index

In person without chronic bronchitis	0.44 ± 0.09
In person with chronic bronchitis	0.52 ± 0.08



PATHOPHYSIOLOGY

Airflow Limitation

Airflow limitation and increased airways resistance may be caused by loss of elastic recoil during passive exhalation due to emphysema by increased collapsibility of small airways through loss of radial traction on airways, or to increased resistance due to intrinsic narrowing of small airways.

Impaired Gas Exchange

Maldistribution of inspired gas and blood flow is always present to some extent. When the mismatching is severe, impairment of gas exchange is reflected in abnormalities of ABG. Small airway narrowing causes a decrease in ventilation of their distal acinus. When alveolar capillaries remain intact, this

result in mismatching of ventilation and blood flow, reduced V/P ratio and mild to moderate hypoxemia, with emphysema, destruction of alveolar walls may decrease alveolar capillary perfusion as well, better preserving V/P matching and P_aO_2.

Pulmonary Circulation

Pulmonary arterial hypertension develops late in the course of COPD, with the development of Hypoxiema (P_aO_2 < 60 mmHg) and usually hypercapnia. It is the major cardiovascular complication of COPD and is associated with RV Hypertrophy[24] and with a poor prognosis in patient with COPD.

Factors contributing to the development of pulmonary arterial hypertension

1. Destruction of the pulmonary vascular bed.
2. Abnormal blood gas tensions.
3. Abnormal pulmonary mechanics.
4. Increased cardiac output.
5. Blood volume changes.
6. Increased blood viscosity.
7. Endothelial abnormalities.

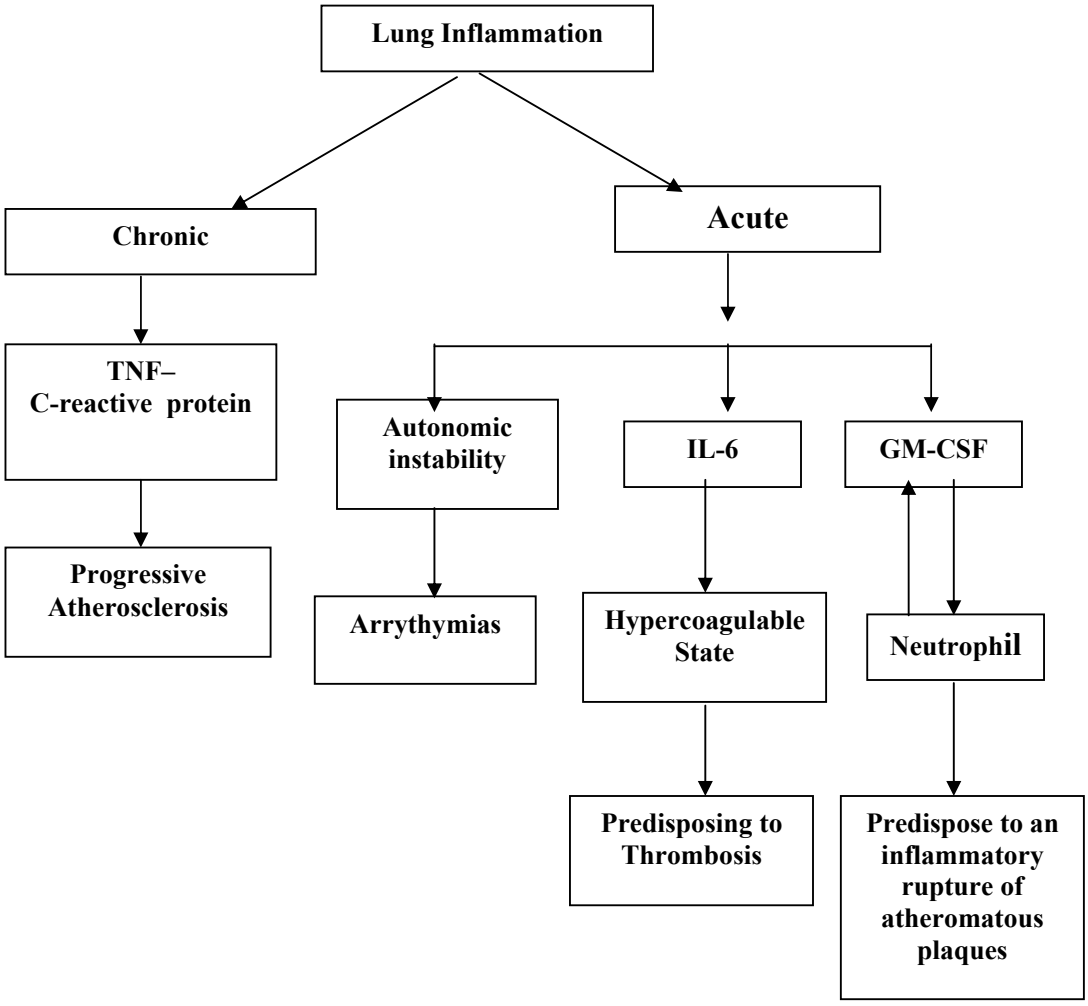
Renal and Hormonal Dysfunction

Chronic hypoxia and hypercapnia increase circulating levels of NE, Renin, aldosterone, AVP. Renal arterial endothelium in COPD patient exhibits

defects similar to those seen in pulmonary arteries shunting blood flow from cortex to medulla and impairing renal functional reserve. All these changes lead to salt and water loads and RV dysfunction.

EFFECT OF COPD ON CARDIOVASCULAR SYSTEM

Chronic Obstructive Pulmonary Disease can contribute to cardiac disease by variety of mechanisms[27,28,52].



(ii) Functional interdependence

Patient with COPD likely stress their heart in number of ways both at rest and with exercise.

Rest	Changes in Lung	Exercise	Cardiac consequences
↑	**Lung Hyperinflation**	↑↑↑↑	**--**
↑	**Work of breathing**	↑↑↑↑	**Need to deliver increased cardiac output**
Normal / ↑	**Intrathoracic pressure**	↑↑↑↑	**Decreased venous return (Cardiac output)**
Normal / ↑	**Pulmonary Hypertension**	↑↑↑↑	**Increased cardiac strain; limited increase cardiac output**

(iii) Cardiac risk factors to consider in patients with COPD

- Hypertension
- Diabetes
- Hypercholestrolemia
- Renal Compromise (GFR < 60 ml/mt)
- Microalbuminemia
- Obesity
- Physical inactivity
- Family History
- Suggested lung assessment

  i. FEV_1

  ii. FVC or FEV_6

❖ **Others**

i. Post bronchodilator FEV_1

ii. Lung Volumes

iii. DLco

iv. Exercise challenge (with or without bronchodilater)

Reduction of Tachyponea, will lead to increase exercise tolerance, reduces the RA(Right Atrium) strain[52].

LABORATORY EVALUATION OF THE PATIENT WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

HEMATOLOGY

Red Blood Cells

Erythrocytosis is seen in certain patients with COPD, as well as in smokers without significant airflow obstruction. A hematocrit at sea level about 52% in men and 47% in women warrants evaluation, because higher hematocrits are seen in less than 5% of normal individuals. Upper normal limits for hemoglobin are 17.7g/dl for men and 15.7g/dl for women.

A normal red blood cell mass with a decreased plasma volume is characteristic of patients with relative (or) spurious erythrocytosis. An increased red blood cell mass with a normal or decreased plasma volume is found in those patients with absolute (or) secondary erythrocytosis, which responds to discontinuation of smoking with oxygen therapy.

Classification of increased Hemoglobin or packed cell volume in the COPD patient

Type of Erythrocytosis	Examples
1. Relative erythrocytosis (decreased plasma volume, normal red cell volume)	Volume depletion – i.e. diuretic therapy, gastrointestinal disease, dehydration. Smokers polycythemia Chronic relative erythrocytosis
2. Absolute erythrocytosis (or) Secondary Erythrocytosis	1. Appropriate Erythropoietin Secretion – i.e. High altitude, abnormal hemoglobin function, smokers' polycythemia, Chronic Obstructive Pulmonary disease (COPD). 2. Inappropriate Erythropietin secretion – i.e. renal disease (Cysts, hypernephroma), cerebellar hemangioblastoma, hepatoma, etc.,
3. Primary Erythrocytosis	Idiopathic

White Blood Cells

Leukocytosis in patients with COPD may result from either a complicating event (e.g. infection) or a therapeutic intervention (e.g. steroid therapy). Blood and sputum eosioniphilia have been associated with a therapeutic response to steroid administration in some series.

Leukocytosis with a marked eosinophilia (> 300 mm^3) suggests a complicating disorder, such as allergic bronchopulmonary aspergillosis, eosinophilic pneumonia, Churg-Strauss vasculitis, or the hypereosinophilic syndrome.

Platelets

Patients with COPD and hypoxemia may demonstrate subtle abnormalities of platelet function. Decreased platelet survival time, shortened regeneration time and increased platelet aggregation with elevations of the plasma beta-thromboglobulin level (an in vivo marker of platelet activation) have all been reported in hypoxemic COPD patients.

CHEMISTRY

Electrolytes

Hyponatremia in patients with COPD can arise in several different ways (mechanisms). Complicating disorders such as lung tumors and pulmonary infection may produce hyponatremia by inappropriate secretion of antidiuretic hormone. Most commonly, however, hyponatremia occurs as a result of salt and water retention.

A second electrolyte abnormality often seen in chronic obstructive pulmonary disease is hypokalemia. Patients with hypokalemia are at increased risk for the occurrence of cardiac arrhythmias and respiratory muscle weakness. Hypokalemia may be present in COPD patients as a result of oral intake, gastrointestinal loss from vomiting or diarrhea, or renal tubular defects with K^+ wasting.

Hypophosphatemia is a frequent electrolyte abnormality in hospitalized patients with chronic obstructive pulmonary disease. Hypophosphatemia usually results from a combination of insults.

Hypomangesemia and hypocalcemia have also been associated with respiratory muscle weakness. Although most frequently a complication of alcohol abuse, hypomagnesemia may also result from the frequent administration of diuretics.

The complete clinical implications of these electrolyte abnormalities have not been firmly established in the COPD patient. The significant effect that electrolyte disturbances may have on respiratory muscle function, however, dictates close monitoring of these variables in the COPD patient.

PULMONARY FUNCTION TEST

Although hundred of different types of disease can affect the lungs. Only a few measurable pulmonary function derangement are found. Identification of the physiological abnormalities present by using PFT narrow the list of possible causes of lung diseasae[25].

Anatomic and physiological changes in the lungs occur early and remain clinically silent for many years. Pulmonary functions are grossly abnormal in symptomatic patients[26].

Ventilatory performances vary widely with body size, age and sex. Tables and nomograms are available which take these variables in to account and display predicted normal values for individuals of particular age and height.

The standard PFT used to measure airway obstruction is the forced expiratory spirometry.

FEV_1 is the volume of air expelled in the first second of maximal forced expiration from a position of full inspiration.

FVC is obtained by continuing forced expiration until no further air can be expelled.

Vital capacity is the volume of air expelled by a maximal expiration by a position of full inspiration.

The relationship between FEV_1 and FVC is clinically very useful as it is to a large extent independent of body size and age.

FEV_1 is reduced in any condition that reduces the vital capacity and when there is diffuse obstruction.

In forced expiration about 75% air is expelled in first second.

Tidal volume is the volume of air that enters and leaves the lung during normal breathing.

INSPIRATORY RESERVE VOLUME

The maximum volume of Air that can be inspired after normal inspiration.

EXPIRATION RESERVE VOLUME

Maximum volume that can be exhaled from the resting level.

RESIDUAL VOLUME

The volume of air still remaining in the lung after maximum volume of air that can be expelled from resting level.

CHARACTERISTIC ABNORMAL LUNG FUNCTION IN OBSTRUCTIVE PULMONARY DISEASE

1. Reduced FEV_1, FVC and PEFR.
2. Relatively greater reduction in FEV_1, than FVC.
3. Increased RV and RV/TLC ratio
4. Uneven distribution of inspired gas
5. Increased non elastic work of breathing
6. Reduced P_aO_2
7. Increased $PaCO_2$
8. Lowered arterial pH during exacerbation

Chronic Respiratory failure : $PaO_2 < 60$ mmHg

$PaCO_2 > 50$ mmHg

While breathing are at sea levels

GOLD CRITERIA FOR COPD SERVERITY

Gold Stage	Severity	Symptoms	Spirometry
0	At risk	Chronic cough, sputum production	N
I	Mild	With less without chronic cough or sputum production	$FEV_1/FVC < 0.7$ and $FEV_1 \geq 80\%$ predicted
II	Moderate	With less without chronic cough or sputum production	$FEV_1/FVC < 0.7$ and $50\% \leq FEV_1 < 80\%$ predicted
III	Severe	With less without chronic cough or sputum production	$FEV_1/FVC < 0.7$ and $30\% \leq FEV_1 < 50\%$ predicted
IV	Very severe	With less without chronic cough or sputum production	$FEV_1/FVC < 0.7$ $FEV_1 < 30\%$ predicted (or) FEV_1 50% predicted plus chronic respiratory failure

An alternative way of looking at faced expiration is to measure both expiratory flow and volume exhaled plotting flow against volume to give a Maximum Expiratory Flow Volume curve (MEFV).

Flow Volume Loops

Expiratory flows at 75% or 50% of VC have been used as a measure of airflow limitation and provide complementary information to the usual volume time plot. There are problems with the reproducibility of these measurements, so that abnormal values must fall to below 50% of the predicted values. Flows

at lung volumes less than 50% of VC were previously considered to be an indicator of small airways function but probably provide no more clinically useful information than measurements of FEV_1. Measurements of flow at fixed lung volumes are very variable in patients with COPD since volume calculated from flow at the mouth does not take account of thoracic gas compression during expiration. The flow-volume loop in severe COPD shows a relatively preserved PEF followed by a rapid decrease in flow after the first 200 – 300 ml, as airways collapse.

PEF can either be read directly from the flow – volume loop measured with a hand-held peak flow meter. The hand held instruments are relatively easy to use and are particularly useful for repeated measurements in asthmatics, since serial measurements during exacerbations or at home can reveal variations in response to therapy or spontaneous diurnal variability. However, in COPD there is little daily change in PEF and many variations are often within the error of the measurement. Although repeated measurements of PEF can be used in place of FEV_1 single measurements are not useful as the variation is so high. There are several theoretical reasons why FEV_1 is a better test than PEF in the diagnosis and assessment of COPD, so that PEF is an inferior measurement of airways obstruction in COPD.

The reasons why FEV_1 recommended as the measurements of choice in COPD

- The FEV_1 is a reproducible and objective measurement. There are well-defined normal ranges that allow for the effects of age, race and sex.

- It is relatively simple and quick to measure and can be measured at all stages of diseases.

- The forced expiratory manoevure records not only FEV_1 but also FVC. An FEV_1/FVC ratio less than 70% is diagnostic of airways obstruction. If the ration is normal (>70%) and the test was performed well, the pattern is not obstructive and the diagnosis is not COPD.

- PEF measurements cannot determine whether values are low because of obstruction or restriction.

- The variance of repeated measurements in the same person is well documented and is low studies of mortality and disability have shown that the FEV_1 predicts future mortality.

- Serial measurements provide evidence of disease progression.

- In COPD the relationship between PEF and FEV_1 is poor.

- PEF may underestimate the degree of airways obstruction in COPD.

Gas Transfer for Carbon Monoxide

DLco values are below normal in many patients with COPD and although there is a relationship between DLco and the presence of microscopic emphysema, the severity of the emphysema in an individual patient cannot be predicted from the DLco. Neither is a low DLco specific for emphysema. Thus a low DLco is suggestive of a significant degree of alveolar destruction, probably as a result of emphysema, although a normal DLco does not exclude a

diagnosis of COPD. The methodology to assess DLco may also influence the result in patients with COPD. The method of Ogilvie and colleagues measures the rate of carbon monoxide uptake during a 10s breath hold and related this to the alveolar volume, derived by adding the inspired volume to the RV measured in a separate helium dilution test. Now, more widely used method is the single breath technique, which uses alveolar volume calculated from helium dilution during the single breath test. This underestimated alveolar volume in patients with severe COPD, producing a lower value for DLco.

Arterial blood gases

Measurement of arterial blood gases is essential in patients with COPD to confirm the degree of hypoxemia and hypercapnia and, in acute exacerbations particularly, to determine the hydrogen ion concentration. It is recommended in patients with an FEV_1 < 40% of their predicted value. It is essential to record the inspired oxygen concentration when reporting blood gases, and it is also important to note that it may take at least 30 min for a change in inspired oxygen concentration to have its full effect on the P_aO_2 because of long time constants for alveolar gas equilibration in COPD.

Pulse oximetry and transcutaneous oxygen tension measurements are increasingly used in intensive care units. They can be useful in measuring changes in oxygenation during an acute exacerbation of COPD, sleep, and activities. However, they should not replace an assessment of blood gas tensions, since measurements of PaCO2 are often required.

Acid-base status can also be assessed from the arterial pH (hydrogen ion concentration) and bicarbonate concentration. From the modified Henderson – Hasselbalch equation, (H+) = kx$PaCO_2$ / (HCO_3-) where (H^+) is the hydrogen ion concentration, K a constant and [HCO_3-] the bicarbonate concentration, increases in $PaCO_2$, which can occur rapidly, can be compensated by renal conservation of bicarbonate, a relatively slow process. Acid-base status, particularly mixed respiratory and metabolic disturbances, can be characterized by plotting values on an acid-base diagram [559]. Such a diagram is useful in apportioning the relative contributions of primary respiratory and metabolic causes of the acid-base disturbance and, when serial values are plotted, the response to treatment.

In COPD of mild to moderate severity Hypoxemia typically occurs without Hypercapnea. In severe COPD, CO_2 retension and severe hypoxemia occurs severity of arterial desaturation more in blue bloaters than pink puffers. Episodes of nocturnal desaturation associated with worsening of pulmonary hypertension.

In nomenclature of acid base disorders P^H, $PaCO_2$, HCO_3 (bicarbonate) are considered. $PaCO_2$ values are normally kept within narrow limits by the respiratory centre, and the Chemo receptors located in the medulla, close to floor of 4^{th} ventricle and in caroid. These receptors are suppressed by chronic Hypoxia, Hypercapnea, secondary to alveolar hypoventilation.

Respiratory acidosis is frequently associated with COPD; Respiratory alkalosis encountered in patient on diuretic therapy, transient hyperventilation.

Reversibility to Bronchodilators

The American, European and British Thoracic Societies (ATS, ERS and BTS) recognize that assessment of reversibility to bronchodilators is an essential part of the investigation and management of patients with COPD. Reversibility tests are important in COPD for several reasons: (a) to help distinguish those patients with marked reversibility who have underlying asthma. (b) because the FEV_1 after bronchodilator is the best predictor of survival. However, there is no agreement on a standardized method of assessing reversibility. Reversibility is usually assessed by measuring changes in FEV_1 or PEF but could also be determined as a change in static lung volumes after bronchodilators, which may explain why some patients have improvement in symptoms with little spirometric change following a bronchodilator.

ELECTROCARDIOGRAPHIC FEATURES

COPD influence the electrical events of the heart in the following respects.

1. The voluminous lungs have an insulating effect and there by diminish the transmission of electrical potentials to the registering electrodes.

2. The heart descends to a lower position within the thorax due to lowering of the diaphragm. This will alter the position of the heart relative to the conventional precordial electrode position.

3. RV and RA become compromised due to reduction of pulmonary vasacular bed. This will result in RVH and dilatation as well as RA enlargement.

ECG pattern are influenced by many factors such as PAP, pulmonary vascular resistance, rotation and displacement of heart by hyper inflated lungs, ABG, myocardial ischemia and metabolic dysfunction[27].

The voluminous lungs impair electrical transmission causing marked diminution of QRS and T waves.

The loss of r or R wave amplitude in the precordial leads are attributed to

a) Low anatomic position of heart

b) Inferiorly and posteriorly directed QRS axis

Right atrial enlargement is manifested by right ward deviation of 'p' wave axis and characteristics 'P' pulmonale.

Frontal plane QRS axis is usually deviated to the right.

Schaffer et al[29] found that 5% patient with COPD had LAD, while 9% had dominant 'S' wave in the three standard leads ($S_1S_{11}S_{111}$ syndrome).

The single most characteristic of COPD is said to be a 'P' wave axis between +70 and $+90^{o}$.

There may be complete and incomplete RBBB.

The presence of RV hypertrophy is mostly reflected by (a) RAD, (b) Prominent terminal S waves in left precordial leads, (c) in advanced case of PHT, the R waves may become inverted in the magnitude in (Rt) precordial leads.

Fishman anoted that[30] the standard criteria for RV enlargement were absent in 2/3rd of patient with COPD who had RVH on post mortem

It has been suggested that where classical RVH changes are absent, diagnosis be based on combination of[30].

a. rs in V_5 V_6
b. RAD
c. QR in a VR
d. `P' pulmonale

Most frequent arrhythmia seen is multifocal artrial tachycardia.

COPD can produce changes in the ECG that mimic MI. A marked reduction or even total absence of anterior QRS forces are most common observation result.

In small r wave or QS complex in precordial lead $V_1 – V_4$.

If there is additional RVH or acute RV dilatation, T wave become inverted in these leads further mimicking MI. Abnormal Q wave or QS complexes can be recorded in leads AVF or Lead I thus mimicking inferior wall (or) lateral wall infarction. If the diagnosis of COPD is known, any ECG showing those features should not be interpreted as showing MI unless there is clinical correlation.

The electrocardiogram (ECG) is abnormal in approximately 75% of patients with significant obstructive airway disease. The characteristic ECG findings in these patients are summarized. Although none of the individual criteria is specific, the simultaneous finding of characteristic P wave and QRS changes strongly supports the presence of underlying COPD.

Electrocardiographic changes in Chronic Obstructive Pulmonary Disease

ECG Changes	Characteristics
P wave	Right ward deviation of the p wave axis; 'p' wave > 2.5 mm in leads II, III, aV_F; prominent negative 'p' wave in lead I
QRS	Tendency for right axis deviation of the QRS vector and marked clockwise rotation of the electrical axis; QRS amplitude in all limb leads < 5 mm; QRS amplitude < 5mm in leads V_5 and / or V_6, or R wave < 7mm in leads V_5 or R wave < 5mm in V_6, R to S ratio < 1 in leads V_5 and / or V_6; R to S amplitude ratio in V_1 < 1; S_1Q_3 or $S_1S_2S_3$ pattern with R to S ratio < 1 in leads I, II and III; incomplete (and, rarely) complete right bundle branch block.
Other	Lead I sign with isoelectric P wave, QRS amplitude less than 1.5 and T wave amplitude less than 0.5 mm; pseudoinfarction pattern with large Q waves or QS in the inferior or precordial leads.

The more vertical P wave axis, characteristic of patients with significant airflow obstruction, results in the biphasic or isoelectic P wave in lead I and / or a V_1. This shift of the P wave axis correlates with the severity of the airflow obstruction in some series. P pulmonale, characterized by peaked P waves (greater than 2.5 mm) in the inferior leads, occurs in patients with more severe airflow obstruction.

The QRS axis is shifted to the right, usually by less than $+90^0$. This shift of the QRS axis may be associated with an $S_1S_2S_3$ pattern. The orientation of the mean QRS axis posteriorly, superioly, and to the right can result in an 'apparent' left axis deviation. An S_2 greater than S_3 to distinguish this finding from true left axis deviation.

Wasserburg and colleagues have observed an electrocardiographic pattern, termed the "pentology of pulmonary emphysema" in patients with advanced emphysema. This pattern consists of the following: (1) Exaggerated P waves in leads II, III and aV_f (2) prominent T-a waves in leads II, III and aV_f (3) vertical cardiac position, which at times may be extreme; (4) clockwise rotation on the longitudinal cardiac axis; and (5) tendency to low voltage, particularly in the left ventricular leads.

Kok-Jensen studied the ECG features of 228 patients with chronic bronchial obstructions. A decreased survival was seen in patients with a QRS axis of $+90^0$ to 180^0 and a p-wave amplitude in lead II of 0.20 mV or greater; only 37% and 42%, respectively, of the patients with these features were alive at 4 years. Smit and colleagues found that a higher P-wave amplitude in lead II and / or S amplitude in lead V_6 was associated with a decreased 5-year survival.

Sputum Analysis

Cellular analysis of the sputum can be helpful in the evaluation of patients with COPD. Macroscopic examination of sputum is often misleading, because both neutrophil and eosinophills produce purulent sputum. Medici and

Collegues have suggested that the sputum of patients with chronic bronchitis undergoes three phases; a stable phase, an infectious phase and a resolution or post infection phase. During acute exacerbations, sputum neutriphils and bronchial epithelial cells increase. The bronchial epithelial cells remain elevated in the post infectious phase, whereas the neutrophils decrease to stable phase levels. Alveolar macrophages, which do not increase during the infectious phase, increase significantly during the resolution period.

A wet preparation of the sputum or an appropriately stained specimen allows detailed analysis of the cellular elements (alveolar macrophages, neutrophils and eosinophils). The cellular analysis helps to determine the adequacy of the sputum specimens and to distinguish between an infectious exacerbation characterized by a neutrophilic predominance and an allergic exacerbation characterized by an eosinophilic predominance (occasionally associated with Curschmann's spirals and charcot-Leyden crystals).

Diplococcus pneumoniae and Hemophilus influenzae are the most common bacterial organisms isolated from patients with increased production of purulent sputum. They are also found as regular inhabitants of the upper respiratory tract of normal individuals. In addition, they are frequently present in the tracheobronchial secretions of asymptomatic COPD patients. Therefore, the significance of isolating these organisms in the COPD patient with chronic bronchitis and purulent sputum, even with "adequate" specimens, is unclear. Transtracheal aspiration represents an alternative technique for obtaining specimens of tracheobronchial secretions for bacteriologic evolution in the COPD patient. The technique involves the insertion of a needle catheter

system through the cricothyroid membrane with aspiration of tracheobronchial secretions. Transtracheal aspiration should only be carried out by trained personnel because of the increased risk of complications associated with the techniques, such as bleeding, infection and subcutaneous emphysema.

Although generally recognized to be more reliable than expectorated sputum, interpretation of the results of cultures of transtracheal aspirates in patients with chronic lung disease is again limited as a result of a high incidence (86%) of positive cultures, even in clinically stable patients. Schreiner and colleagues, using transtracheal aspirates in 76 patients with chronic sputum production, found that 80% of the aspirates in 76 patients with chronic sputum production, found that 80% of the aspirates grew Hemophilus influenzae or Diplococcus pneumoniae[31]. Haas and associates, studying patients with chronic bronchitis, compared three methods for the evaluation of tracheobronchial secretions in patients with chronic sputum production; oropharyngeal sampling, transtracheal aspiration, and bronchoscopy. They found a high degree of correlation in the culture results using all three techniques. As expected, patients with chronic bronchitis most commonly grew H. influenzae and D.neumoniae, regardless of the sampling method.

Finally, bronchoscopy and related techniques, inlcuidng transbronchial lung biopsy, protected catheter brush specimens, and bronchoalveolar lavage, are available for the evaluation of infection in the COPD patients. Because of the increased risk of morbidity and mortality with these procedures, they are generally reserved for the COPD patient with undiagnosed pneumonia or for

the immunocompromised host. The risks and benefits of these techniques have been reviewed elsewhere.

Despite the many techniques available for sputum analysis of the COPD patient, the most appropriate indications and technique for microbiologic analysis have yet to be determined. The consistence isolation of identical organisms, regardless of the sampling technique or clinical status of the patient, has prompted some clinicians to conclude that sputum microbiologic evolution in the absence of pneumonia is unrewarding.

In addition to microbiologic criteria, biochemical characteristics of sputum have been proposed for the evaluation of COPD patients. Inflammatory bronchial secretions may contain elevated levels of deoxyribonucleic acid (DNA0, lacate dehydrogenase (LDH), fibrinogen, and albumin. Shockely and colleagues have suggested that levels of 11S (locally produced) and 7S (Serum-derived) IgA are increased in infectious sputum. In addition, the free secretory piece of IgA seen in noninfected sputum is apparently absent in infected specimens. The value of these biochemical parameters in the evaluation and treatment of patients with COPD remains to be determined.

Other proteins such as albumin, the immunoglobulins, transferring, AAT, $alpha_2$ – macroglobulin and $alpha_1$ – antichymotrypsin may also be present. Under conditions of chronic bronchial irritation, these proteins may exist in a partially fragmented or denatured form. Albumin and AAT appear to enter lung secretions by passive diffusion, whereas $alpha_1$ – antichymotrypsin and $alphs_2$ – macroglobulin are secreted locally.

Corpulmonale

Pulmonary Heart Disease (i.e. corpulmonale) refers to cardiac dysfunction resulting from altered structure or function of lung. Since lungs are interposed in the cardiovascular circuit between the Right Ventricle (RV) and left side of the heart. Alterations in lung structure or function will selectively affect the right side of the heart, most often result from COPD. World Health Organization defined chronic corpulmonale as "Hypertropy, with eventual dilatation of right ventricle resulting from disease affecting the function and / or structure of lung, except when these pulmonary alterations are the result of disease that primarily affect the left side of the heart or congenital heart disease. Acute corpulmonale is a disorder in which right ventricle is dilated and muscular wall is stretched and thin. Most often result from pulmonary embolism[27,34].

In Delhi, India, where a large segment of population lives under conditions of severe air pollution and incidence of corpulmonale estimated to be 16%, less common causes of corpulmonale are diffuse interstitial lung disease, tuberculosis with extensive destruction of parenchyma and conglomerate fibrosis, sleep apnoea syndrome.

Common predisposing factors for corpulmonale are arterial hypoxemia, respiratory acidosis which leads to pulmonary hypertension (PH) and corpulmonale. Generally, up to 14% of patients with COPD suffering from secondary pulmonary hypertension.

The diagnosis is generally based on electrocardiographic criteria. The classic determinant of RVH, developed from patient with congenital heart disease; includes (i) a right axis shift of QRS (> 110); (ii) an R to S ratio in V_1 > 1 and (iii) a R to S ratio in V_6 < 1. However, these have proven to be relatively poor criteria for diagnosis of corpulmonale in patient with COPD.

Some electrocardiographic findings may be seen in patients with emphysema in the absence of right ventricular hypertrophy (RVH). These involve 'p' pulmonale; S1, S2, S3 pattern, and the left ward shift of the transitional zone.

The presence of (i) RSR or QR pattern in V_1 (ii) marked clockwise rotation of electrical axis (iii) a frontal plane QRS of 110^o or more (iv) large Q waves or QS waves in inferior, mid precordial leads (v) ST, T changes right precordial or inferior leads are more suggestive of RVH in those with COPD.

Kilcoyne and associates have suggested progressive change in ECG occurs in response to hypoxemia arterial saturation of < 80% and mean pulmonary artery pressure 25 or more.

These changes consists of:

1. Inverted, biphasic or flattened 'T' waves in the right precordium.
2. Mean electrical axis of QRS shift 30^o or more to right side of the patient's usual axis.
3. ST segment become depressed in lead II, III, aV_F
4. RBBB complete or incomplete

These abnormality frequently variable with degree of hypoxemia. If pulmonary hypertension persisted, the right ward rotation of the QRS axis and the 'T' wave changes in the right precordial leads remained.

If pulmonary function was not reversed with therapy, the true right axis deviation (a frontal plan axis > 90^{o}) and increased R wave voltage in the right precordial leads developed. These abnormalities tended to be non-reversible.

The classic view of the development of right ventricular hypertrophy (RVH) in patients with COPD is that reduction of pulmonary vascular bed and hypoxia induced pulmonary vasoconstriction, increased pulmonary vascular resistance, leading to pulmonary hypertension.

Non invasive techniques

Non-invasive techniques, such as echocardiography, radio nudeotide imaging, HRCT, MRI are used to confirm the diagnosis of pulmonary hypertension complicating COPD. M-Mode echocardiography is of limited usefulness because the hyperinflation of the chest that occurs with COPD interferes with adequate visualization of the right ventricle.

Two-dimensional echocardiography (2D echo), however, permit visualization of both right ventricular chamber and pulmonary artery dimensions. The Echocardiographic parameters of pulmonary hypertension includes analysis of motion of pulmonary valve, right ventricular anterior wall thickness, pulmonary artery size, right sided systolic time interval ratio and the slope of the contrast echoes through pulmonary valve.

Limitations in the use of echocardiography to assess the status of pulmonary hypertension are poor penetration of ultrasound in these patients particularly in patient with emphysematous changes.

The systolic pulmonary artery pressure could be estimated accurately with continous wave Doppler ultrasound (CWD) from the peak velocity of a TR jet.

MRI helps to assess right ventricle (RV), left ventricle (LV) mass, end diastolic volume (after the R-wave of ECG), ejection fraction (EF). Marked RV hypertrophy accompanied decreased RV end diastolic volume. The hypertrophy is classified as concentric type and is consistent with radiological characteristics of emphysema i.e., patients with narrow vertical heart. Increased RV dimensional seen with severe COPD patients.

The adequacy of radio nudeotide investigation of the heart with thallium – 201 imaging depends on the muscle wall and the blood flow to the organ to allow visualization. The non-dominant right ventricle is usually not visualized in most patients studied with this technique. The right ventricle of patients with COPD shows right ventricular enlargement and / or hypertrophy. Right ventricular visualization with thallium – 201 imaging suggest the presence of pulmonary hypertension. Measurement of right ventricular ejection fraction by radio medeotide imaging may be another useful test for the non-invasive diagnosis of pulmonary hypertension in COPD.

Prognosis of COPD

COPD has variable natural history. It is not having specific indicators to grade the severity. Spirometry has definitive role in assessing the severity prognosis inversely related to age and directly related to post bronchodilator FEV_1. BODE scoring helps in assessing the mortality rate at 52 months which includes body mass index (BMI) obstruction (FEV_1 % predicted), Dyspnoea, exercise, score of 0 – 2 caused 10%; 7 – 10 causes 80% mortality rate at 52 months.

MATERIALS AND METHODS

50 patients attending outpatient department in Government Stanley Hospital during the period of November 2006 – June 2007 were studied.

Inclusion Criteria

1. All patient with chronic obstruction airway disease whose FEV_1 less than 70% of total FVC.

Criteria for chronic bronchitis

a. History of chronic cough with exacerbation followed by breathlessness.

b. Clinical examination showing diffuse crepitation and ronchi in both lung fields.

Criteria for emphysema

a. History of chronic breathlessness with recent onset of cough with expectoration.

b. Clinical examination showing increased AP diameter, diminished chest expansion, Hyper resonant note on percussion, decreased cardiac dullness, elicitation of hepatic dullness at a lower plane and dinished vocal fremites, vocal resonance, breath sound.

c. Radiologically

i. Flattening of diaphragmatic domes

ii. Long and narrow cardiac silhouette

iii. Increased translucency and widening of intercostals spaces.

Patient in acute exacerbations

1. Worsening of cough and sputum production
2. Worsening of breathlessness
3. Change in colour of sputum

Patient with age group of 22 – 86 years with duration of illness ranging from one to fifteen years at different stages of disease were studied.

Exclusion criteria

1. All cases with pneumonia or bronchiectasis on chest x ray
2. HIV positive patient
3. Patient with lung malignancy
4. Acute pulmonary tuberculosis

RESULTS

- The study included 50 patients of age 22 – 86 years
- Among these, 30 patients belonged to Emphysema, 20 belonged to chronic bronchitis group.
- Although most patients have combination of both group.

AGE WISE DISTRIBUTION OF THE ABOVE PATIENTS

Age	Chronic bronchitis	Emphysema	Total	Percentage
< 40	2	0	2	4%
41 – 50	6	8	14	28%
51 –60	8	16	24	48%
61 – 70	2	4	6	12%
71 – 80	2	1	3	6%
> 80 years	0	1	1	2%

SEX WISE DISTRIBUTION OF THE PATIENTS

Sex	Chronic bronchitis	Emphysema	Total	Percentage
Male	18	30	48	96%
Female	2	0	2	4%

In this study, most of the patients with COPD were only males.

DISTRIBUTION OF PATIENTS ACCORDING TO SOCIO ECONOMIC STATUS

Socio Economic status	Total	Percentage
High	2	4%
Intermediate	10	20%
Low	38	26%

HISTORY OF SMOKING AMONG 50 PATIENTS OF COPD

Smoking History	Chronic bronchitis	Emphysema	Total	Percentage
Moderate smokers	8	12	20	40%
Chain smokers	8	16	24	48%
Non Smokers	4	2	6	12%

88% of patients with COPD were past smokers. Only 12% were non smokers.

FAMILY HISTORY OF COPD

Family History	Chronic bronchitis	Emphysema	Total	Percentage
Present	**6**	**0**	**6**	**12%**
Absent	**14**	**30**	**44**	**88%**

Family History of Obstructive airway disease present only in 12% patients.

SPIROMETRIC EVALUATION OF PATIENTS WITH COPD

FEV_1 of predicted	Chronic bronchitis	Emphysema	Total	Percentage
50 – 80%	**3**	**6**	**9**	**18%**
30 – 49%	**10**	**16**	**26**	**52%**
< 30%	**7**	**8**	**15**	**30%**

Majority of patients 52% had FEV_1% of predicted is 30 – 49%.

CHEST X-RAY FINDING AMONG 50 PATIENTS

X-ray changes	Chronic bronchitis	Emphysema	Total	Percentage
Emphysematous changes	2	26	28	56%
Increased broncho vascular markings	16	4	20	40%
Cardiomegaly	1	0	1	2%
PAH (Rt.decending pulmonary artery > 16 mm)	1	0	1	2%

ECG FINDINGS AMONG 50 PATIENTS

ECG Changes	Chronic bronchitis	Emphysema	Total	Percentage
1.'p' wave > 2.5 mm	10	12	22	44%
2. QRS axis > 90	6	7	13	26%
3. 'R' wave in V_1 > 7 mm (or) R/S in V_1 > 1	6	3	9	18%
4. R/S in $V_5 \leq 1$	5	8	13	26%
5. RV strain	6	3	9	18%
6. RBBB	2	1	3	6%
7. Poor 'R' wave progression	3	8	11	22%
8. LI sign	2	4	6	12%
9. QRS in limb leads < 0.5 mv	6	8	14	28%
10.MAT	3	2	5	10%

ARTERIAL BLOOD GAS CHANGES (ABG) AMONG 50 PATIENTS

ABG Changes	Total No. of Patients	Percentage
Normal	45	90%
Respiratory Acidosis	5	10%
Respiratory alkalosis	0	0%

ECHOCARDIOGRAPHIC CHANGES AMONG 50 PATIENTS

Echo changes	Total No. of patients	Percentage
PH	--	0%
RV dilation with pulmonary Hypertension (PH)	2	4%
Normal	48	96%

CORRELATIVE ANALYSIS OF ABG, ECHOCARDIOGRAPHY, SPIROMETRY

FEV_1	Respiratory acidosis	RV dilatation
50 – 80%	**--**	**--**
30 – 49%	**2**	**1**
< 30%	**3**	**2**

DISCUSSION

In this study of 50 patients with COPD; 30 (60%) patients belonged to a group with predominant emphysema feature. 20 patients (40%) belonged to the predominant chronic bronchitis feature even though in some of the above patient there was overlap between the two group having a mixed features.

AGE

They all belonged to different age groups. Mostly they were between 40 to 80 years.

Highest age → 86 years

Lowest age → 22 years

Commonest age group according to various studies is between middle and late adult life[31].

In India, the disease is mostly enumarated in males over 40 years who have been chronic and heavy smoker[26].

Increasing age is an important risk factor but it has not been possible to prove that this is the result of aging perse rather than cumulative effect of explosive to environmental stresses[32].

In this study COPD is mostly seen from 4^{th} to 6^{th} decade.

SEX INCIDENCE

Regarding sex incidence, males are more affected than female.

In this study, 96% case were male this is in according with the world literature[31] COPD is not common in female[32].

Male preponderance was probably due to the repeated explosive smoking habits and atmospheric pollution. However, the incidence of COPD had been said to be increasing in female also in West.

SOCIO ECONOMIC STATUS

There is no single classification of socio economic status. In our study patients were divided into 3 groups based on occupation.

1. High - Professionals
2. Intermediate - Partial skilled occupations
3. Low - Unskilled occupational

In our study, most of the patients (76%) belong to low socio economic status. It is likely that the effect of socio economic status is mediated by associated factors such ass over crowding, frequency of respiratory illness, nutrition, availability of medical care, etc., Socio economic status appears important in some studies but not in others. Hence, socio economic status might be considered as additional provocative factor than an inherent risk factor of COPD[45].

SMOKING

History of smoking elicited. Excluding female almost all makes gave a history of chronic smoking either cigarette or beedi. They were divided into:

1. Moderate smokers → > 10/day for > 10 years

2. Chain smokers → 20/day for > 15 years

In our study COPD was present only 6 non smokers (12%). Of these, 2 of them were females. Although cigarette smoking is generally regarded as the dominant risk factor. Cigarette smoking is not a prerequisite in all definition of COPD, since COPD can occur in non smokers[34].

FAMILY HISTORY

In this study, 6 patients give family history of wheezing (12%). These patients have feature of Asthma with feature of chronic bronchitis. Although COPD patients were divided into chronic bronchitis and emphysema some patients have features with Asthma. They were classified as a group called asthmatic bronchitis[6]. According to one study familial tendency does not appear to be an important risk factor for airway obstructive diseases[35].

SPIROMETRY

FEV_1 / FVC ratio is grossly reduced in-patient suffering from chronic bronchitis. These patients were divided into various severities by **GOLD CRITERIA[2]** according to FEV_1 as a percentage of predicted value.

	Severity	FEV_1% Predicted
i.	Mild	50 – 80%
ii.	Moderate	30 – 49%
iii.	Severe	< 30%

In this study, most patients (82%) have FEV_1 / FVC ratio of < 50%. This is in accordance with the principle most patients become symptomatic only when FEV_1 falls below 50%[2].

CHEST X RAY FINDING

In our study, a total of 28 patients showed emphysematous change, which consist of low flattened diaphragm, decreased vascularity in the periphery of lung, tubular heart[36,37]. In this 28 patient 2 belonged to chronic bronchitis group. The accuracy of diagnosis emphysema on the plain chest film increased with severity of disease and has been reported as being 50 – 80% accurate in patients with moderate to severe disease[36]. However, the sensitivity has been reported as being as low as 24% in patient with mild to moderate disease.

20 patients showed increased bronchovascular marking most of them were predominantly of chronic bronchitis group. Here increased bronchovascular markings means they could be seen up to the periphery of lung field with a coarser appearance. 1 patient showed radiographic evidence of pulmonary – artery hypertension evidenced by diameter of right descending pulmonary artery greater than 16 mm[38].

One patient showed cardiomegaly. These patient was carefully screened for coexisting condition like systemic hypertension and valvular heart disease. However, such condition were not present in the above mentioned one patient with prominent chronic bronchitis features. So, cardiomegaly may be probably due to gross enlargement and clockwise rotation of right ventricle.

ECG CHANGES

The single most characteristic ECG feature is 'p' wave axis between +70 - +90 and 'p' wave amplitude > 2.5 mm[39].

In our study, both these changes were present in 44% of patients respectively. Patient with 'p' pulmonale also exhibited marked reduction in FEV_1 ratio below 50%[42].

KDK – Jensea studied the ECG features of 228 patients with chronic bronchial obstruction. A decrease survival was seen in patients with a QRS axis of +90 and + 180 and 'p' wave amplitude in lead II of 0.2 MV or greater.

Frequently instead of full blown pattern of RV hypertrophy and strain with tall 'R' waves in V_1 an intermediate pattern is seen with deep 'S' waves across the precordial leads $V_1 – V_2$[4]. rS pattern in the chest leads corresponds with a large posteriorly directed portion of the horizontal vector loop (Walsh et al 1960) and is clearly attributed to Emphysema. Carvaso G et al 1991[41] conducted a study to evaluate the correlation of ECG changes and spirometric parameters in corpulmonale secondary to COPD.

They performed the study with 56 patients with COPD and they developed an ECG scoring system (0 – 6). It consists of:

a. QRS axis > 90^o
b. 'p' wave > 2.5 mm
c. R wave in V_1 > 7 mm in R/S in V_1 > 1
d. R/S V_5 < or equal to 1
e. RV strain pattern
f. RBBB

They noted a increased relationship between ECG score and FEV_1 / FVC.

In our study, the above score study was correlated with FEV_1/FVC ratio. Patients who had score more than 3 were taken into account. There is an increase correlation between FEV_1 / FVC ratio and ECG score system is noted i.e. as ECG score increases FEV_1 / FVC ratio and increases pressure over load on right ventricle.

Severe COPD may be complicated by MAT[43] (Multifocal Atrial Tachycardia). Significant obstructive airway disease is recognized in 30 – 80% of patients presenting with this rhythm abnormality. In our study MAT has been found in 6 patients (12%).

Arterial Blood Gas

Arterial Blood Gas analysis was done for all patients. Out of 50 patients, 5 patients showed respiratory acidosis which constitutes 10% of total study population; 6% (3) of patients were belonged to severe COPD stage. 4% (2)

patients were belonged to moderate COPD stage. None of the mild COPD stage patients showed Arterial Blood Gas abnormality[51].

Echocardiography

Right ventricular dilatation, pulmonary hypertension, left ventricle systolic function were considered.

In this study, out of 50 patients, 4% (2) showed RV dilatation with normal LV systolic function. They were belonged to severe COPD group.

According to Pinar Yildiz et al, right ventricular dysfunction directly correlated with severity of COPD grading[52].

With correlation of FEV_1 predicted %, arterial blood gas analysis, echocardiograpahic changes are prevalent in patients with FEV_1 of < 50%[53,54].

It consistent with Boussuges et al, who demonstrated increase in RV diameter in severe COPD with pronounced chronic bronchitis changes and arterial hypoxemias[57].

Scope for future study

- Evaluation of right atrial (RA) strain as reflected by changes in 'p' wave amplitude and vector in patients with COPD immediately before and after beginning treatment of exacerbations. As per study conducted by Navaid Asad et al, 'p' wave amplitude in COPD decreases once an acute exacerbation subsides[53].

- Prognostic role of ECG in CCP (Chronic Corpulmonale) gaiven by Antonelli et al[54] which includes

    1. S1, S2, S3 pattern
    2. RAO (Rt atrial overload)
    3. RVH
    4. RBBB
    5. Low Voltage QRS
    6. S1 Q3 pattern

    2 of the 6 ECG changes of CCP associated with shorter survival rate in COPD patients.

- Effect of passive smoking or second hand smoke exposure in spouses, close contacts of smoking personal by using serum cotinine level, urine 4 methyl nitrosamine level.[58]

- COPD mortality has increased in recent years and by the year 2020 it is expected to become the third leading cause of death in the World[55]. Hence, further study is required.

CONCLUSION

From out study of 50 patients of COPD, following conclusions were derived.

1. 60% of patients belonged to predominantly emphysema group and 40% belongs to predominantly Chronic Bronchitis group.

2. COPD patient mostly were in the age group 4^{th} to 6^{th} decade.

3. 96% of patients were males.

4. 70% of COPD patients were from low socio economic status.

5. History of smoking is present in 88% of the patients.

6. Family History was present only in 12%.

7. Radigraphic evidence of pulmonary artery hypertension were present in 2%.

8. Commonest ECG changes were ‘p’ pulmonale pattern (44%).

9. Multifocal atrial tachycardia in ECG was present in 10% of patients.

10. ABG, Echocardiographic spirometric correlation showed respiratory acidosis 4% in moderate COPD; 6% in severe COPD patients. RV dilatation 4% seen in severe grade of COPD.

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PROFORMA

1. Name :
2. Age :
3. Sex :
4. Occupation :
5. Income :
6. Address :
7. OP / IP No. :
8. Complaints:

    Breathlessness : Duration

    Cough with expectoration :

    Sputum – Amount :

    Wt. Loss, Colour loss of appetite :

    Fever :

    Wheezing :

    Diabetes Mellitus, Hypertension :

    Any other complaints :

9. Previous History of

    Cough

    Smoking – Mod → > 10/day > 10 Yrs

    Chain → > 20/day > 15 yrs

    Wheezing and Asthma

10. Other relevant past History, family history

11. Clinical findings

General Examination
Chest Findings

12. Investigations

1. TC
2. DC
3. ESR
4. Hb%
5. Blood Sugar

13. Serum

a. Urea
b. Creatinine
c. Electrolytes

14. Urine

a. Albumin
d. Sugar
e. Deposits

15. Mx test done and positive cases excluded

16. PFT done and those with $FEV_1 < 70\%$ of FVC are included in study

17. Chest X-ray – AP view / Lateral View

18. Arterial blood gas analysis

19. Cardiovascular status was assessed in all cases along with radiological and ECG means to exclude associated disease like Hypertension, valvular heart disease, etc.,

20. HIV I & II